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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,709	DOYLE ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7 and 9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 10/19/06, has been entered.

Amended claims 3, 4, 7, 9, 10, and 11, filed 10/19/06, are acknowledged.

Claims herein under examination are 1-4, 6-7, and 9-11.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-7, and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1 (line 8), 4 (line 11), 7 (line 7), and 11 (line 7) recite the phrase "unattendedly micro dissecting" which is vague and indefinite. It is unclear what Applicant means by this phrase. It is unclear by what or by whom the micro dissecting is being unattended. Clarification

of this issue via clearer claim wording is requested. Claims 2-3, 6, and 9-10 are also rejected due to their dependency from claims 1, 4, and 7.

Applicants argue that "unattendedly micro dissecting" is intended to mean "micro-dissection without any selection by an investigator" and point to paragraph 35 of the specification. This statement is found unpersuasive as "unattended" has not been defined in the specification to relate to any absence of selection. Paragraph 35 recites "a UV laser adapted to the application end of a microarray-creation robotic apparatus" which "allows for unattended section incising of a large number of specimens". It is noted that this paragraph does not mention or preclude the absence of any selection by an investigator. For example, a selection can take place before using an unattended robotic arm. Applicants argue that the lack of a reference to what or whom is not attending the micro dissecting does not make the claim indefinite. This is a conclusory statement without factual support as to why this rejection would be considered improper. Applicants argue that it is clear from the language that the micro dissection of a serial section does not require active selection of parts of the serial section to be micro dissected. This statement is found unpersuasive because while this limitation is not required, it is not precluded either.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-7, and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heppelmann et al. (Journal of Microscopy, Vol. 156, Pt. 2, 1989, pages 163-172) in view of Cole et al. (Nature Genetics supplement, Vol. 21, 1999, pages 38-41), Farr et al. (P/N 5,811,231), Emmert-Buck et al. (Science, Vol. 274, 1996, pages 998-1001), and Lemelson (P/N 6,058,323).

Heppelmann et al. describe methods for creating multidimensional morphological reconstruction of biological tissue data characterizing a biological tissue sample by cutting histologically thin sections of tissue in two sets of alternating serial sample sections (page 163, lines 1-12) as stated in claims 1, 4, 7, and 11. Heppelmann et al. describe performing these three dimensional reconstructions with graphical techniques and computer-aided methods (page 163, lines 13-14) featuring a spatial matrix of image data with x, y, and z axes as seen in Figure 4, which represents mapping image data obtained from the first set of alternating serial sections onto a coordinate system as well as volume image data correspondence, as stated in claims 1, 4, 7, and 9-11. Heppelmann et al. describe cutting the second set of sections (for ultrastructural examination) with an ultracut ultramicrotome and mounting them on single-slot grids to be further examined (page 164, last paragraph) which represents microdissecting each serial section

to create a set of microdissected section samples for each serial section of the second set, as stated in claims 1, 4, 7, and 11. Heppelmann et al. describe examined 3-D structures were fitted and projected onto the lines of a coordinate system of the z-dimension according to their vertical position which was calculated from the section thickness as well as connecting the same structures in their vertical projection revealed in a side view projection diagram (page 165, third paragraph and Figure 2) which represents assigning a unique code (calculation) to each section sample indicating tissue space coordinates and specific range in the morphological space matrix, as stated in instant claims 1, 7, 9, 10, and 11. Heppelmann et al. describe the sections were mounted in sequence on mesh grids (page 165, lines 12-14) which is reasonably interpreted to be associating each incised section sample with unique set of indices as the mesh grids have x and y coordinates, with each individual sample placed in a known location. Heppelmann et al. describe histologically-staining the first set of sections and adding a coverslip (page 164, fifth paragraph) which could be used for light microscopy reconstructions (page 163, lines 4-5) as stated in claim 4. Heppelmann et al. describe that the second set of tissue sections are covered with a synthetic membrane which is then further cut (page 164, paragraphs 6 and 7), as stated in claim 4.

Heppelmann et al. do not teach using a microarray and biological data analyses type which involve mRNA as elected in the species elections. Heppelmann et al. do not teach linking these data to each coded microdissected tissue sample in the multidimensional morphological matrix. Heppelmann et al. do not describe unattendedly microdissecting, analyzing tissue with monoclonal antibodies, obtaining gene expression data, and superimposing them on the

multidimensional morphological matrix of image data to display correlating values of data with corresponding locations on the matrix.

Cole et al. describe a web-based, visual system for allowing querying of gene expression profiles while viewing associated anatomy and histopathology (page 40, col. 2 (third paragraph) which represents a system of creating morphological reconstruction of biological data characterizing a tissue, as stated in instant claims 7 and 11. Cole et al. describe a model for integrating three dimensional expression data obtained using a microarray involving mRNA analysis (page 38, abstract (lines 5-6), and col. 1 (lines 1-4)) which represents methods and systems for analyzing sections providing a plurality of biological characteristics of the coded micro-dissected samples, as stated in instant claims 1, 3, 7, and 11. Cole et al. discuss cutting tissue in transverse cross-sections (representing X and Y dimensions) available for micro-dissection and recutting adjacent serial sections in the Z dimension (page 40, col. 1, lines 7-14) which are used to create a multidimensional morphological spatial matrix of image data as seen in Figure 1 including letters A – G for different sections which represents micro-dissecting across each serial section of a set with uniquely coded (lettered) sections, as stated in instant claims 1, 4, 7, 9, and 11. Cole et al. describe the transverse sections have been annotated with the types and location of histopathology present (Figure 1 caption) wherein the annotation for the sections represent uniquely coded sections. Cole et al. discuss the placement of tissue on slides (page 40, col. 1, lines 11-12) and other newly developed fixation and embedding strategies (page 39, col. 2, lines 15-16). Cole et al. describe methods of preparing microarrays from micro-dissected cells (page 40, col. 1, lines 19-25 and 37-39). Cole et al. discuss that the above processes allows for the determination of exact physical relationships between morphological

data (one set) on which to overlay gene expression data (second set)(page 40, col. 1, lines 14-17 and col. 2, lines 16-24) as well as annotation on tissue sections (Figure 1 and its caption) which represent superimposing biological data of the micro-dissected section sample upon volume image data indicated by code assigned to the sample of the morphological tissue space matrix, as well as obtaining and analyzing biological data, and linking data characterizing each sample to the location, as stated in claims 1, 4, 7, and 11. Cole et al. describe viewing this information on computers and displaying a data chart in three dimensions (page 40, col. 2, lines 26-38) which represent spatially mapping the biological data characterizing each micro-dissected section sample of the second set onto the multidimensional morphological tissue space matrix from the first set, as stated in claim 1. Cole et al. show images of stained tissue sample sections obtained from light microscopy (Figure 1, molecular view) as stated in claim 4. Cole et al. do not teach unattendedly microdissecting, superimposing analyzed RNA data on the multidimensional morphological matrix of image data, analyzing tissue with monoclonal antibodies, and correlating data with corresponding locations on the matrix.

Farr et al. describe a method of measuring biological data, particularly as gene expression levels from specific organs of animal tissues to characterize and identify cellular and subcellular effects of potential toxins on an animal cell (col. 2, lines 52-62 and col. 6, lines 15-23). Farr et al. describe starting experiments with tissue sample and cell lines (col. 6, lines 15-23). Farr et al. describe the results graphically in Figures 1-11 (col. 31, lines 5-6) which consist of multidimensional (3D) representations of the biological data. As can be seen in the Figures 1-11, each data column is indexed and to a particular set of conditions, such as the expression of an enzyme under control of different promoters in the presence of varying concentrations of a test

compound (col. 3, lines 24-67). Each of these particular set of conditions was tested with genetic material bound to a solid support membrane which was placed on a 96-well plate referring to rows and columns (col. 20, lines 53-67; col. 26, lines 9-11; and col. 29, line 49 to col. 30, line 31) which represents coded micro-dissected section sample holders which allowed for proper coding and correlation of each set of test conditions to the resulting graphical representations described above, as stated in claims 1, 4, and 6. Farr et al. describe an autoradiograph taped to a 96-well plate holder to align the radioactive dots with the holes of the plate holder so that each well is quantified according it each well position (col. 28, lines 23-27 and col. 29, line 49 to col. 30, line 31) which is a form of image data superimposed and visually transferring of grid elements to the corresponding sample holder, providing sample holders indicating identity of the sample sections and coordinate location, and analyzing each grid element with expression data, as stated in instant claims 1 and 4. Farr et al. describe correlating the results and creating profiles (col. 28, lines 30-32) as stated in claim 6. Farr et al. describe analyzing assays using antibodies to detect proteins (col. 19, lines 55-67 and col. 20, lines 1-14) with expression levels being regulated by interactions between surface receptors and ligands (col. 4, lines 52-55) as stated in claim 2. Farr et al. describe the method to include detecting levels of mRNA (col. 20, lines 25-67) as stated in claim 3. Farr et al. do not teach unattendedly microdissecting or physically transferring incised grid elements.

Emmert-Buck et al. describe a film or membrane applied to the surface of a tissue section on a glass slide (abstract, lines 3-5), which represents mounting and covering a second set of sections with a micro dissection membrane, as stated in instant claim 4. Emmert-Buck et al. describe automatic microdissection without manual procedure and a laser applied to specific

locations of the film to procure specifically targeted cells that can then be transferred (page 998, third column, first full paragraph and abstract, lines 5-9) which represents unattendedly microdissecting and suggests transferring specific micro-dissected tissue and selecting only particular subsections.

Lemelson describes the idea of generating images of tissue which may be computer processed and analyzed to generate multiple cross-sectional views such as parallel slice images with code signals indicating coordinate locations of those structures (col. 9, third paragraph) which represents assigning a unique code to tissue sections indicating tissue space coordinates, as stated in instant claims 1, 4, 7, and 11. Lemelson does not describe the coded microdissected section holders.

Cole et al. state that gene expression microarrays hold great promise in studies of human disease states (abstract, line 1). While some technical issues have yet to be addressed, other precise measurement techniques are at hand to view molecular anatomy of normal cells and their disease counterparts (Cole et al., abstract). Farr et al. state the need for quick, inexpensive and reliable alternatives to toxicity testing in animals (col. 2, lines 11-13) such as using techniques of measuring transcription and translation levels of genes (col. 2, lines 52-62). Farr et al. state the kits and methods of their invention yield rapid and direct information about the nature of a compound's action on mammalian cells (col. 3, lines 12-21). Farr et al. also state that the basic construction of the kits, processes, and products of their invention can be altered to provide other embodiments (col. 32, lines 14-21). Heppelmann et al. state that complex morphological structures cannot be fully appreciated without three-dimensional reconstruction (page 163, lines

15-16). Heppelmann et al. point out that stacking of contoured sections for reconstruction is an old technique that is now aided by graphical methods and computers (page 163, lines 16-21).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to utilize improved methods of comparison of multidimensional graphic data expression representation to microscopy data, as stated by Cole et al. (page 40, col. 2, lines 21-28) via three-dimensional histological techniques to increase understanding of complex morphological structures as stated by Heppelmann et al. (page 163, lines 15-16 and page 171, lines 11-13), using simple and precision tissue extraction with laser capture microdissection that minimizes contamination, as stated by Emmert-Buck (abstract and page 998, col. 3, lines 2-6 and 12-15), and displaying the gene expression data in easy-to-read uniquely coded tissue sections, slides, and three-dimensional graphs as shown by Farr et al. (such as Figure 1) and Lemelson, because these rapid, exact and efficient techniques would improve accuracy and visual representation for easy interpretation of correlations between the data types available to scientists at the time of the invention (Emmert-Buck, abstract; Farr et al., col. 2, lines 11-13; Cole et al., abstract and page 38, col. 1, first paragraph).

The person of ordinary skill in the art at the time the invention was made would have been motivated to study complex 3-D morphological structures of Heppelmann et al. (page 163, fifth paragraph) combined with the entire tissue studies including gene expression profiles of the different sections, as stated by Cole et al. in order to discover genotypic changes in tissue that may not be apparent phenotypically to provide new insights in cancer biology at the molecular level (Cole et al., page 38, col. 1, first paragraph and page 38, col. 2, second paragraph).

The person of ordinary skill in the art at the time the invention was made would have been motivated to discover genotypic changes in tissue sections from Heppelmann et al. and Cole et al. via coded microarray plates of Farr et al. (col. 29, lines 49 to col. 30, line 31) in order to organize, interpret, and gain insights from large amounts of gene expression data generated by complex biological systems, as stated by Cole et al. (page 38, col. 1, first paragraph), and to precisely identify and characterize biological effects on certain tissues, as stated by Farr et al. (abstract, lines 1-12).

The person of ordinary skill in the art at the time the invention was made would have been motivated to create tissue sections of Heppelmann et al., Cole et al., and Farr et al. with the automated laser capture microdissection as stated by Emmert-Buck et al. in order to provide a ease, precision, and efficiency in a rapid one-step procurement of selected targeted human cells from a section of complex, heterogenous tissue (Emmert-Buck et al. abstract and page 998, col. 2, second paragraph).

The person of ordinary skill in the art at the time the invention was made would have been motivated to analyze tissue sample sections of Heppelmann et al., Cole et al., Farr et al., Emmert-Buck with the computerized imaging system with cross sectional tissue views indicating coordinate locations of the structures of Lemelson (col. 9, third paragraph) in order to efficiently query gene expression profiles while viewing associated anatomy and histopathology which will further understanding of molecular events that underlie tumor development for producing new diagnostic, prognostic, and therapeutic targets for the benefits of patients (Cole et al., page 40, col. 2, third and fourth paragraphs).

One of ordinary skill in the art would have expected success of combining the three-dimensional reconstruction techniques of Heppelman et al. with Cole et al.'s visual system for allowing query of gene expression profiles while viewing associated anatomy and histopathology because both involve a variety of tissue sectioning methodologies for three dimensional reconstructions (Heppelmann et al., summary; Cole et al., page 39, col. 2, last paragraph).

One of ordinary skill in the art would have expected success of combining the tissue section analyses of Cole et al. with the tissue analyses of Farr et al. because both use microarrays for gene expression analyses which allows a quick and expensive alternatives to toxicity testing in animals (Farr et al., col. 2, first paragraph).

One of ordinary skill in the art would have expected success of combining the laser capture microdissection technique of Emmert-Buck et al. with the tissue samples of Farr et al. because Emmert-Buck emphasizes the next generation of molecular analysis methods involving tissue selection need to be miniaturized and automated for clinical molecular diagnostic testing of gene expression (Emmert-Buck, page 998, col. 1, first paragraph and abstract), such as the gene expressions studied by Farr et al.

One of ordinary skill in the art would have expected success of combining the computer image analysis with coordinate locations of Lemelson with the visually oriented system of Cole et al. as both use the coordinate locations to orient views to the anatomic location, such as tumors, which allows for a rapid query of profiles across a spectrum of samples as stated in Cole et al. (Figure 1).

Thus, Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson, make obvious and motivate the limitations of claims 1-3, 6-7, and 9-11.

Applicants summarize Heppelman et al., Cole et al., Farr et al., Emmert-Buck et al., and Lemelson. Applicants summarize the 35 USC 103(a) rejection. Applicants argue the prior art references do not suggest or teach the steps recited in claims 1, 4, 7, and 11 and summarize these claims. This statement is found unpersuasive as these limitations are taught by the prior art of record, as clearly stated in the rejection above. Applicants reiterate parts of the 35 USC 103(a) rejection and argue that Heppelmann et al. do not teach unattendedly micro dissecting a serial section into a set of micro dissected section samples or of assigning a code to indicate the location of a coded micro dissected section sample in a multidimensional spatial matrix. This statement is found unpersuasive as this is a 35 USC 103 rejection, such that not every limitation needs to be recited by a single reference. Heppelmann et al. recite micro dissecting samples, Emmert-Buck et al. recite steps including unattendedly micro-dissecting samples, Lemelson et al. recite steps of assigning code (see rejection above). Applicants argue that Heppelmann et al.'s incising of serial samples would be contrary to the teaching of the instant invention since the serial sections are analyzed by a microscope. This statement is moot as analysis via a microscope is not recited or precluded in the instant claims. Applicants argue that incising or micro dissecting the sections would destroy their utility for that purpose. This statement is unpersuasive as it is a conclusory statement without factual support. Furthermore, Heppelmann et al. describe further ultrastructural examination (page 164, last paragraph). Applicants reiterate the argument that Heppelmann et al. do not teach assigning a code to a coded micro dissected section samples and the lack of motivation to assign codes to the micro dissected tissue samples. These statements are found unpersuasive as Lemelson recite steps of assigning code. In addition,

motivational statements have been provided in the rejection above, and Applicants failed to provide sound reasoning as to why this motivation would be considered improper. Applicants summarize part of prior art rejection regarding the Cole et al. reference. Applicants argue that Cole et al. do not discuss micro dissecting a serial section into a set of micro dissected samples or assigning code to indicate the location of a coded micro dissected section sample in a multidimensional spatial matrix. This statement is found unpersuasive as Heppelmann et al. and Cole et al. describe micro dissecting while Cole et al. and Lemelson describe assigning code. Applicants summarize Cole et al. and argue that Cole et al. do not unattendedly micro dissect sections into a multi-dimensional spatial matrix of coded micro dissected samples as required by instant claim 1. This statement is found unpersuasive as Cole et al. need not recite every limitation of the claim, since this is a 35 USC 103 rejection instead of a 35 USC 102 rejection. For example, the "unattended" limitation is taught by Emmert-Buck et al. Applicants recite a portion of Emmert-Buck et al. and argue that they do not suggest unattendedly micro dissecting a serial section into a set of micro dissected section samples or assigning a code to indicate the location of a coded micro dissected section sample in a multidimensional spatial matrix. This statement is found unpersuasive as Emmert-Buck et al. need not recite every limitation of the claim, since this is a 35 USC 103 rejection instead of a 35 USC 102 rejection. These limitations are recited by the prior art references as already discussed above. Applicants argue that the techniques of "visualizing the tissue microscopically, and selectively adhering the cell of interest to the film" described in the reference do not suggest or teach the claimed feature. It is noted that the abstract and page 998 describe mounting and covering sections as well as unattendly micro dissecting which are the limitations for which Emmert-Buck et al. reference was relied

upon in the rejection. Applicants argue that because the paragraph immediately before the first full paragraph of column 3 on page 998 states cells are selectively adhered to the film, the fact that no manipulation is required is inapposite to whether the micro dissection is unattended. This statement is found unpersuasive as the instant claims only recite the micro dissection step is unattended ("no manual micro dissection" on page 998, col. 3), and this step does not preclude any other type of selection before or after the micro dissection. Applicants argue that Lemelson do not teach unattendedly micro dissecting a serial section sample or a code assigned to each micro dissected section sample indicating the location of the coded micro dissected sample in the multidimensional matrix. This statement is found unpersuasive as Lemelson need not recite every limitation of the claim, since this is a 35 USC 103 rejection instead of a 35 USC 102 rejection. For example, the "unattended" limitation is taught by Emmert-Buck et al. The Lemelson reference is relied upon to describe assigning a unique code to tissue sections indicating tissue space coordinates.

Applicants summarize MPEP 2143. Applicants argue that the fundamental principle of operation of Heppelmann et al, Cole et al., and Emmert-Buck et al. is that an area of interest is selected for further analysis from a section being viewed whereas the instant claims involve serial sections of a biological sample that are unattendedly micro dissected into serial sections without any selection, and the micro dissected sections are further analyzed. This statement is found unpersuasive as the instant claims do not recite a "without any selection" limitation. The only unattended step in the recited claims is the micro dissecting step which is taught by Emmert-Buck et al. who describe automatic micro-dissection without manual procedure (page 998, third column, first full paragraph and abstract). Applicants argue a "what if" scenario that

in Cole et al. if an investigator needed data that had not been previously selected, dissected, and analyzed it would be necessary to go back and dissect another cell population for analysis which might not be possible. This statement is moot as the rejection is not based on "what if" scenarios, but rather what is specifically stated in the claims. Applicants summarize Cole et al., Emmert-Buck et al. and Heppelmann et al. and argue the proposed combination would change the principle of operation of the primary reference and render it inoperable. Applicants argue that if the serial section of Heppelmann et al. were micro dissected it could not be used for the next step of ultra-sound analysis since the structure of the serial section would have been destroyed. This statement is found unpersuasive as Heppelmann et al. describe further ultrastructural examination after incision (page 164, last three paragraphs).

Applicants summarize MPEP 2143.01. Applicants argue that the claimed features are not taught by the cited references. This statement has already been found unpersuasive for the reasons given above. Applicants argue that there is no motivation in the references to combine the features as recited in the pending claims. This statement is found unpersuasive as motivational statements have been provided at the end of the 35 USC 103(a) rejection. Applicants argue that none of the listed motivations meet the recited claim limitations. This statement is found unpersuasive as the motivational reasoning for combining references need not come from the claim limitations or have the same purpose as the instant invention. Applicants summarize the motivational statement on page 13 of the previous Office Action and argue that the statement teaches away from the claimed combination above. This statement is found unpersuasive as procurement of selected target human cells is not teaching away from the claimed invention that does not even recite selection or the lack thereof.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heppelmann et al. (Journal of Microscopy, Vol. 156, Pt. 2, 1989, pages 163-172) in view of Cole et al. (Nature Genetics supplement, Vol. 21, 1999, pages 38-41), Farr et al. (P/N 5,811,231), Emmert-Buck et al. (Science, Vol. 274, 1996, pages 998-1001), and Lemelson (P/N 6,058,323) as applied to claims 1-3, 6-7, and 9-11 above, and further in view of Bogen et al. (P/N 6,281004).

Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson, make obvious and motivate the limitations of claims 1-3, 6-7, and 9-11, as described in the 35 USC 103 rejection above. These references do not describe coded micro-dissected section holders.

Bogen et al. describe microscope slides with tissue sections containing labels containing surgical accession number, patient name, and a barcode (col. 7, last paragraph) which represents a coded tissue section sample holder, as stated in instant claim 4.

The person of ordinary skill in the art at the time the invention was made would have been motivated to code tissue sample sections of Heppelmann et al., Cole et al., Farr et al., Emmert-Buck, and Lemelson with a coded tissue section sample holder of Bogen et al. (col. 7, last paragraph) in order to efficiently compare and contrast large datasets across multiple patients and samples, as stated by Cole et al. (page 40, col. 2, third paragraph).

One of ordinary skill in the art would have expected success of combining the coded tissue sample holder with the tissue sections of Bogen et al. with the tissue sections of

Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson as it would reliably monitor quality control within the laboratories to ensure accuracy, as stated by Bogen et al. (col. 1, first paragraph).

Thus, Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson, and Bogen et al., make obvious and motivate the instant invention.

Applicants argue that the arguments made above are incorporated by reference herein. It is noted that the above arguments are unpersuasive for the reasons given above. Applicants summarize instant claim 4 and Bogen et al. Applicants argue that the samples affixed to the matrix in Bogen et al. are different concentrations of antigens and have no relationship to a spatial image of any kind. This statement is found unpersuasive as Bogen et al. need not recite every limitation of the claim, since this is a 35 USC 103 rejection instead of a 35 USC 102 rejection. Bogen et al. is relied on for the coded micro-dissected section holders (col. 7, last paragraph). Applicants summarize Lemelson and argue that there is no disclosure relating to assigning codes to actual micro dissected section samples indicating the location of the section samples in a multidimensional spatial matrix. This statement is found unpersuasive as Lemelson need not recite every limitation of the claim, since this is a 35 USC 103 rejection instead of a 35 USC 102 rejection. These limitations are recited by the prior art references as already discussed above.

Applicants' arguments are deemed unpersuasive for the reasons given above.

Conclusion

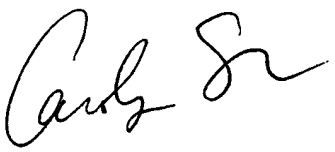
No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811.

October 31, 2006



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Examiner
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